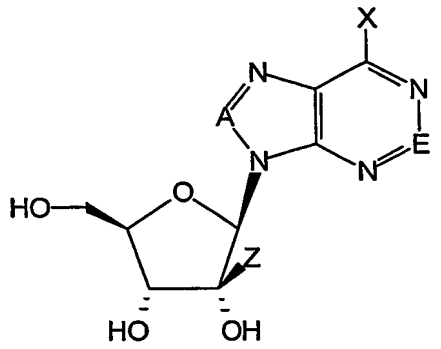
AMENDED CLAIMS

[received by the International Bureau on 19 Mars 2003 (19.03.03) ;
original claims 1-31 replaced by
new claims 1-31 (5 pages)]

1. A compound according to Formula 1



Formula 1

in which Z is selected from the group consisting of an alkyl, an O-alkyl, an alkenyl, an alkynyl, and CN, wherein the alkyl, the alkenyl, or the alkynyl is optionally substituted with a halogen or OH;

A is CH or N, and E is C-R_6 or N, such that (1) when A is CH then E is C-R_6 or N, and (2) when A is N then E is CH;

X is NR_1R_2, $NR_2NR_3R_4$, $NR_2N{=}NR_3$, $NR_2N{=}CHR_3$, $NR_2N{=}O$, $NR_2C(=O)NR_3R_4$, $NR_2C(=S)NR_3R_4$, $NR_2C(=NH)NR_3R_4$, $NR_1C(=O)NR_2NR_3R_4$, NR_2OR_3, ONHC(O)O-alkyl, ONHC(O)O-aryl, ONR_3R_4, SNR_1R_2, $SONR_1R_2$, or $S(O)_2NR_1R_2$;

wherein R_1, R_2, R_3, and R_4 are independently H, alkyl, substituted alkyl, O-alkyl, cyclic alkyl, heterocyclic alkyl, alkoxy, alkaryl, aryl, heterocyclic aryl, substituted aryl, acyl, substituted acyl, $S(O)_2$-alkyl, NO, NH_2, or OH; and

R_6 is H, NH_2, halogen, N_3, NHR_1, $NHCOR_1$, NR_1R_2, $NHSO_2R_1$, $NHCONHR_1$, $NHCSNHR_1$, CH_2NHR_1, CHR_1NHR_2, $NHNH_2$, CN, alkyl, alkenyl, alkynyl, CH_2-aryl, CH_2-heterocycle, halogen, OH, or SH; and

wherein combination of the radicals A, E, X, and Z confer antiviral activity against HCV to the compound.

2. The compound of claim 1 wherein A and E are CH, Z is CH_3 and wherein X is NR_1R_2.

3. The compound of claim 2 wherein R_1 is CH_3, NH_2, or H, and wherein R_2 is CH_2CH_2OH, $CH_2CH_2NH_2$, OCH_3, CH_3, or OH.

4. The compound of claim 1 wherein A and E are CH, Z is CH_3 and wherein X is $NHNR_3R_4$.

5. The compound of claim 4 wherein R_3 is H, or CH_3, and wherein R_4 is H, CHO, $C(O)CH_3$, $C(O)OCH_3$, $S(O)_2CH_3$, or CH_3.

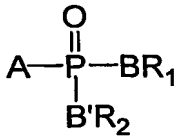
6. The compound of claim 1 wherein A and E are CH, Z is CH_3 and wherein X is ONHC(O)O-alkyl or ONHC(O)O-alkaryl.

7. The compound of claim 6 wherein ONHC(O)O-alkyl is $ONHC(O)OC(CH_3)_3$, and wherein ONHC(O)O-alkaryl is ONHC(O)O-CH_2-phenyl.

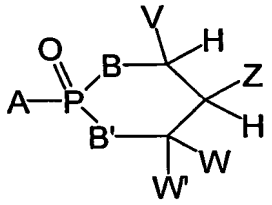
8. The compound of claim 1 further comprising a moiety covalently coupled to at least one of the C2'-atom, C3'-atom, and C5'-atom, thereby replacing the OH group at the at least one of the C2'-atom, C3'-atom, and C5'-atom, and wherein at least part of the moiety is preferentially cleaved from the compound in a target cell or target organ.

9. The compound of claim 8 wherein the moiety comprises a cyclic phosphate, a cyclic phosphonate, or a cyclic phosphoamidate.

10. The compound of claim 8 wherein the moiety has a structure according to Formula M1 or Formula M2



M1



M2

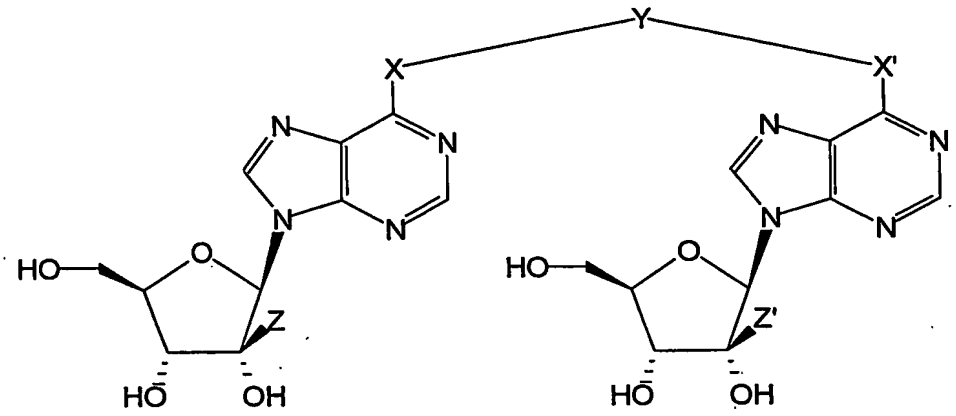
wherein A in M1 or M2 is O or CH_2 and replaces the 5'-OH group of the compound of Formula 1;

B and B' are independently O or NH, and where at least one of B and B' is NH then at least one of R_1 and R_2 is an amino acid that forms a peptide bond with the N atom of the NH, respectively, and where at least one of B and B' is O then at least one of R_1 and R_2 is $CH_2CH_2SC(=O)$t-butyl or $CH_2OC(=O)$iPr; and

V, W, and W' are independently hydrogen, alkyl, alkenyl, alkynyl, aryl, chlorophenyl, alkaryl, each of which is optionally substituted, and Z is hydrogen, CHWOH, CHWOCOW', SW, or CH_2aryl.

11. The compound of claim 1 further comprising a phosphate group covalently coupled to the C5'-OH group to form a phosphate ester.

12. A dinucleoside compound according to Formula 2



Formula 2

wherein X and X' are independently NH, N-alkyl, or N-substituted alkyl;

Y is $(CH_2)_{1-10}$, $(CH_2CH_2O)_{1-3}$, $(CH_2CH_2S)_{1-3}$, a heterocyclic ring, or an aromatic ring; and

Z and Z' are independently selected from the group consisting of an alkyl, an O-alkyl, an alkenyl, an alkynyl, and CN, wherein the alkyl, the alkenyl, or the alkynyl is optionally substituted with a halogen or OH.

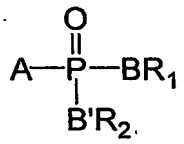
13. The compound of claim 12 wherein Z is CH_3, and wherein X is NH.

14. The compound of claim 13 wherein Y is $(CH_2)_{1-10}$.

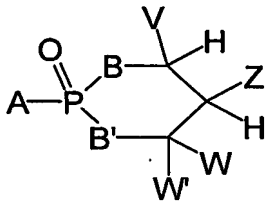
15. The compound of claim 12 further comprising a moiety covalently coupled to at least one of the C2'-atoms, C3'-atoms, and C5'-atoms, thereby replacing the OH group at the at least one of the C2'-atoms, C3'-atoms, and C5'-atoms, and wherein at least part of the moiety is preferentially cleaved from the compound in a target cell or target organ.

16. The compound of claim 15 wherein the moiety comprises a cyclic phosphate, a cyclic phosphonate or a cyclic phosphoamidate.

17. The compound of claim 15 wherein the moiety has a structure according to Formula M1 or Formula M2



M1



M2

wherein A in M1 or M2 is O or CH_2 and replaces at least one of the 5'-OH groups of the compound of Formula 2;

B and B' are independently O or NH, and where at least one of B and B' is NH then at least one of R_1 and R_2 is an amino acid that forms a peptide bond with the N atom of the NH, respectively, and where at least one of B and B' is O then at least one of R_1 and R_2 is $CH_2CH_2SC(=O)$t-butyl or $CH_2OC(=O)$iPr; and

V, W, and W' are independently hydrogen, alkyl, alkenyl, alkynyl, aryl, chlorophenyl, alkaryl, each of which is optionally substituted, and Z is hydrogen, CHWOH, CHWOCOW', SW, or CH_2aryl.

18. The compound of claim 12 further comprising a phosphate group covalently coupled to at least one of the C5'-OH groups to form a phosphate ester.

19. A pharmaceutical composition comprising a compound according to claim 1, claim 10, claim 12, or claim 17, wherein the compound is present at a concentration effective to reduce viral propagation of a virus in a patient infected with the virus.

20. The composition of claim 19 wherein the virus is selected from the group consisting of an HCV virus, an HRV virus, an RSV virus, an HIV virus, and an HBV virus.

21. The composition of claim 19 further comprising a second pharmacological molecule.

22. The composition of claim 21 wherein the second pharmacological molecule comprises an interferon.

23. A method of treating a viral infection in a patient comprising administering a compound according to claim 1, claim 10, claim 12, or claim 17 to the patient in an amount effective to reduce viral propagation.

24. The method of claim 23 wherein the compound is a compound according to claim 1 and wherein the virus is an HCV virus.

25. The method of claim 23 wherein the compound is a compound according to claim 10 and wherein the virus is an HCV virus.

26. The method of claim 23 wherein the compound is a compound according to claim 12 and wherein the virus is an HCV virus.

27. The method of claim 23 wherein the compound is a compound according to claim 17 and wherein the virus is an HCV virus.

28. A method of reducing viral propagation in a cell infected with a virus, comprising presenting the cell with a compound according to claim 1, claim 10, claim 12, or claim 17 to the cell in an amount effective to reduce viral propagation.

29. The method of claim 28 wherein the virus is selected from the group consisting of an HCV virus, an HRV virus, an RSV virus, an HIV virus, and an HBV virus.

30. The method of claim 29 wherein the compound is converted in the cell to a metabolite that reduces viral propagation.

31. The method of claim 30 wherein the metabolite comprises a phosphate group that is covalently coupled to the C5'-atom via an ester bond with the C5'-OH group.